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<b>(54) Title:</b> USE OF MENTHYL-2-PYRROLIDONE-5-CARBOXYLATE AS AN INSECT REPELLENT  <b>(57) Abstract</b>  <p>The use of menthyl 2-pyrrolidone-5-carboxylate as an insect repellent, usually by application to a substrate or into an air space. The menthyl 2-pyrrolidone-5-carboxylate can be used as a composition, which may be perfumed. A useful composition comprises a mixture of menthyl 2-pyrrolidone-5-carboxylate and a known insect repellent or a compound shown to be an effective insect repellent on a test described herein.</p>		

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## USE OF MENTHYL-2-PYRROLIDONE-5-CARBOXYLATE AS AN INSECT REPELLENT

**Field of Invention**

The present invention relates to the use of a menthyl ester as an insect repellent, to  
5 compositions containing the menthyl ester and to a method of repelling insects.

**Background**

Insects have long been known as a nuisance and, for some insect genera, as a health  
hazard. Mosquitoes, for instance, are a proven vector of diseases, and the genus *Aedes*  
10 in particular is associated with yellow fever, dengue, encephalitis and malaria  
(Encyclopaedia Britannica). Although the problems may be reduced at source with the  
use of DDT and other chemical sprays in the breeding areas, fears over the persistence  
of chlorchemicals combined with increasing mosquito resistance to control chemicals  
(e.g. insecticides) have led to a reappraisal of the magnitude of the nuisance and the  
15 hazard. Physical barriers to the insects are not always possible, e.g. in the open air,  
where some form of personal repellent is necessary.

It is also a feature of recent times that the more environmentally-aware public tend to  
question the safety of many chemicals which were formerly taken for granted. One of  
20 these is the well-known personal insect repellent N,N-diethyl-m-toluamide (abbreviated as  
DEET, and commercially available as Delphone<sup>TM</sup>). This was originally seen as the natural  
successor to the parent molecule, N,N-diethylbenzamide which was found to be strongly  
insect repellent but also irritating to human skin (McCabe et al., (1954), J. Org Chem. 19,  
493-498). Fears over possible allergenicity, disclosed in European Patent Application  
25 No. 167266 (Angus Chemical Company), as well as aversion to some of the physical  
properties of this compound such as oiliness and odour, have led to the search for less  
hazardous and more aesthetically acceptable methods of repelling insect pests,  
particularly mosquitoes.

**30 Review of the prior art**

Certain compounds have long been known to possess insect deterrent properties, some of  
this information coming from what might be termed "folk knowledge". These materials  
include widely-known substances such as Citronella, Tolu and Peru Balsams, Eucalyptus  
oils, Huon Pine and other similar oils [M. Bouvier, International Frag. Co-ord. 29 October  
35 1976]. Other materials known for their deterrent properties include those having  
camphoraceous odours, such as Camphor itself, Cypress oils, Galbanum etc. [H&R  
Contact, 36, 1984].

A more scientific approach to the properties of these natural sources has been undertaken by various researchers, such as Lemberkovics et al. [Acta Pharmaceutica Hungarica, 57, (1987) 133-142], Nahrstedt [Planta med. 42(4), 313-32 (1981)], and Popescu [Chim. Anal. (Bucharest), 2(1), 59-61 (1972)] who investigated the effects of Walnut Leaf oil. Kumbu and DiPhanzu [Plant Med. Phytother. 16(1), 23-6 (1975)]  
5 investigated the deterrent effect of a range of Eucalypts against a selection of insect pests.

The popularly-used DEET has also been studied in comparison, and in conjunction, with  
10 a range of ingredients by various researchers. Nishimura et al. [Kagaku to Seibutsu, 27(8), 4886-6 (1989)] investigated the possible synergy of Eucalyptus citriodora and menthanediols with DEET. Solvents such as diethyl phthalate, dimethyl phthalate and dibutyl phthalate are also well known, and these provide the basis for commercial repellents which do not contain DEET, and are also cited in Kirk-Othmer Encyclopedia of  
15 Chemical Technology [3rd Edn., Vol. 13, 476ff]. Canadian patent 1 230 826 (1988) uses a combination of Citronella or Lavender oils, 2-ethylhexanediol and dimethyl phthalate.

Repellent chemicals may be classified into two main groups: general deterrents and species-specific deterrents. Substances known to deter one species have been known to  
20 serve as an attractant to another. An example of this is the use of a mixture of citronellol and eugenol against clothes moths and Anthrenus beetles, described in German patent application DE 3 901 341A [published 1990, Detia Freyberg GmbH]. The latter ingredient, Eugenol, is considered to be a general insect attractant [Kirk Othmer Encyclopedia of Chemical Technology, cited above]. DEET, however, is considered to be a general, or  
25 broad-spectrum, insect repellent. Materials potentially useful as insect repellents are frequently tested against mosquitoes, in particular against the genus Aedes. These materials may also act as general insect repellents.

PCT Application WO 96/08147 discloses the use of a number of different compounds as  
30 insect repellents and also a method by which the repellency of compounds to insects can be reliably tested.

UK Patent GB 1 567 496 discloses a number of terpene esters of 2-pyrrolidone-5-carboxylic acid which are useful in anti-inflammatory topical compositions. These esters  
35 are effective as long lasting physiological coolants and their efficacy is believed to be due to enzymatic hydrolysis on skin that ensures a low level of hydrolysed terpene alcohol (e.g. menthol), which provides a coolant effect, and pyrrolidone carboxylic acid, a natural moisturising factor which conditions the skin.

### Summary of the Invention

5 It has now been surprisingly found that the menthyl ester of 2-pyrrolidone-5-carboxylic acid is an effective insect repellent under conditions in which the above-mentioned hydrolysis is not believed to occur. It has also been shown that the ester is a more effective insect repellent than its hydrolysis product, menthol, and the superior repellency is maintained for at least 1 hour after application to a substrate.

10 Consequently, the invention comprises the use of menthyl 2-pyrrolidone-5-carboxylate as an insect repellent.

Menthyl 2-pyrrolidone-5-carboxylate is commercially available under the Trade Mark QUESTICE but it has not heretofore been recognised as an insect repellent.

15

In another aspect, the invention provides a method of repelling insects from an object or an airspace, comprising application to the object or into the airspace, of an effective amount of menthyl 2-pyrrolidone-5-carboxylate. Typically the object is a human body.

20 The menthyl 2-pyrrolidone-5-carboxylate used as an insect repellent in accordance with the invention can be used in the form of a composition which contains components other than menthyl 2-pyrrolidone-5-carboxylate. In one embodiment, the composition is a perfumed composition.

25 Preferably, the menthyl 2-pyrrolidone-5-carboxylate composition defined above is used to repel biting insects, such as mosquitoes, particularly members of the genus Aedes.

The composition used in the invention, whether perfumed or not, preferably contains at least 0.05% by weight, more preferably at least 0.5% by weight, and most preferably at  
30 least 2.0% by weight of menthyl 2-pyrrolidone-5-carboxylate. Compositions containing not more than 10% by weight of menthyl 2-pyrrolidone-5-carboxylate have been shown to be effective insect repellent compositions.

35 Compositions used in accordance with the invention preferably constitute, or comprise, personal products or cosmetics for use on the skin and/or hair. Examples of such products include fine fragrances, colognes, skin creams, skin lotions, deodorants, talcs, bath oils, soaps, shampoos, hair conditioners and styling agents.

Alternatively, compositions used in accordance with the invention may constitute, or be comprised in, household products such as: air fresheners (including "heated" air fresheners in which insect repellent substances are released upon heating e.g. electrically, or by burning [e.g. joss-sticks, candles]), hard surface cleaners or laundry products (e.g. laundry detergent-containing compositions and conditioners).

Preferably the cosmetics, personal products and household products defined above comprise between 0.1% and 10% of a composition used in accordance with the invention.

- 10 The compositions used in the invention may comprise additional materials to produce desired products such as pleasing perfumes with useful repellent activity. Other materials which may be present in the compositions (at concentrations from 0 to 99.95 % by weight) include fragrances, solvents, diluents and fixatives known in the art, such as:
- Aldehyde C11 (Undecylenic Aldehyde); Aldehyde iso C11 (GIV); Allspice oil; Allyl cyclohexyl propionate; Amyl salicylate; Amylcinnamic aldehyde; Anethole; Anisic alcohol ;
- 15 Anisic aldehyde; Applinal (Q); Bay oil; Benzyl acetate; Benzyl benzoate; Benzyl cinnamate; Benzyl propionate; Benzyl salicylate; Bourgeonal (Q); Brahmanol; Camphor powder synthetic; Cedarwood Virginion; Cedrenol; Cedryl acetate; Celestolide (IFF); Cineole; Cinnamic alcohol; cinnamic aldehyde; Cinnamon Leaf Oil; Cinnamyl acetate; cis-
- 20 3-Hexenol; Citral; Citronella oil; Citronellal; Citronellol; Citronellyl acetate; Citronellyl oxyacetaldehyde; Clove oil; Coriander oil; Coumarin; Cuinic aldehyde; Cyclamen aldehyde; Decanal; 9-Decenol; Dibenzyl ether; Dibutyl phthalate; Diethyl Phthalate; Dihydromyrcenol; Dimethyl anthranilate; Dimethyl phthalate; Dimyrcetol (IFF); diphenylmethane; Diphenyl oxide; Dimethyl benzyl carbonyl acetate; Dodecanol;
- 25 Dodecanal; Elemi oil; Ethyl methyl phenyl glycidate; Ethyl cinnamate; Ethyl safranate (Q); ethyl vanillin; Eugenol; Evergreen oils (Pine oils etc.); gamma-Nonalactone; gamma-undecalactone; Cardamide (Q); Geraniol; Geranium bourbon; Geranyl acetate; Geranyl formate; Gum Benzoin; Heliotropin; Herculyn D (HER); Hexyl benzoate; Hexylcinnamic aldehyde; Hydratropic aldehyde dimethyl acetal; Hydroxycitronellal; Hydroxycitronellal
- 30 dimethyl acetal; Indole; iso Bornyl acetate; Isolongifolanone; Isopropyl myristate; Isocyclocitral (GIV, IFF); Jasmacyclene; Jasmin oil; Lavandin Abrialis; Lavender oil; Lilial (GIV); Linalol; Linalyl acetate; Maceal (Q); Menthol Laevo; Methyl anthranilate; Methyl cedryl ketone; Methyl dihydrojasmonate; Methyl ionone; Methyl ionone alpha iso; Methyl myristate; Methyl naphthyl ketone; Methyl salicylate; Moss treemoss; Musk ketone;
- 35 Neocaspirene (Q); Nerol; Nerolin Bromelia; Neryl acetate; Nonanal; Oakmoss absolute; Octanol Olibanum resinoid; para-Cresyl phenylacetate; para-Methoxyacetophenone; Patchouli oil; Peppermint oil; Petitgrain oil; 2-Phenoxyethanol; Phenoxyethyl iso butyrate; Phenylethylacetate; Phenylethyl alcohol; Phenylethyl butyrate; Phenylethyl phenylacetate;

Pimento oil; Pinene, alpha; Para-tert. butyl-cyclohexyl acetate; Resinoid Benzoin Siam; Rose oil; Rosemary oil; Sandalwood oil; terpineol; Tetrahydrolinalol; Tetrahydromuguol (IFF); Thyme Red; Undecanal; Vanillin; Verbena oil; Vetyvert Bourbon; Yara and Ylang ylang.

5

Compounds are obtainable from the suppliers as indicated below: for those compounds labelled "(Q)" - Quest International, "(IFF)" - International Flavours & Fragrances, Inc., "(GIV)" - Givaudan, "(HER)" - Hercules B.V.

- 10 Other active and non-active materials may be present, such as:  
acidic mucopolysaccharides and their salts, Aesculus hippocastanum, aloe barbadensis  
Mil (Aloe Vera Linne),  $\alpha$ -hydroxycarboxylic acids,  $\alpha$ -ketocarboxylic acids, amide  
derivatives, amino acids, amphiphilic cyclodextrin derivatives,  $\beta$ -sitosterol, carboxy vinyl  
polymer water soluble salts, carboxymethyl cellulose, carrageenan, chitin, chitosan,  
15 cholesterol, cholesterol fatty acid ester, collagen, dicarboxylic acid monostearyl esters, di-  
fatty acid glycerol esters, digalactosyl diglyceride, ersterol, ethanol, extract of Swertia  
japonica Makino, fatty acids, fatty acid citrate esters, fatty alcohols, ginseng extract,  
glucose esters of higher fatty acids, guar gum, gum arabic, Hamamelidaceae (Hamamelis  
Virginiana Witch hazel), hyaluronic acid, hydrochyloesterol, hydroxybenzoic acids,  
20 isomaltose, isopropyl alcohol, lactose, lanosterol, lipids extracted from the biomass of  
microorganisms, yeasts, moulds and bacteria, liposomes, locust bean gum, low  
molecular acidic mucopolysaccharides and their salts, low molecular weight humectant  
components, maltose, mineral oils, mineral powders, monocisalkenoic acid,  
mucopolysaccharides, mycosterol, N-acyl lysines, N-isostearyl lysine, N-lauroyl lysine, N-  
25 myristyl lysine, N-palmitoyl lysine, N-stearoyl lysine, natrium type bentonite, natural or  
synthetic aminoacid with protein or peptide bonds, NMF ingredients, nonvolatile silicones,  
oil agents, oil matter, oligosaccharides, organic acids, pantothenic acid and its  
derivatives, petroleum jelly, phosphatidyl ethanolamine, phosphatidylcholine,  
phospholipids, polysaccharides, polyvinyl alcohol, polypeptides, proteins, raffinose,  
30 saponins, sodium hyaluronate, sources of linoleic acid, sterols, sterol esters, stigmasterol,  
sucrose, sugar esters of higher fatty acids, sulphatide, sunscreens, surfactants, talc,  
thymosterol, tocopherol, mono-, di- or tri-glycerides, vitamins and analogues, vitamin E  
and/or its ester compounds, volatile silicone fluids, water-soluble moisture-retaining  
agents, water-soluble polymers and waxes.

35

Menthyl 2-pyrrolidone-5-carboxylate can be used as the sole insect repellent in a composition or may be used in combination with other compounds which are effective insect repellents.

A further aspect of the invention comprises a mixture of menthyl 2-pyrrolidone-5-carboxylate with a known insect repellent. Known insect repellents which are suitable for use in a mixture with menthyl 2-pyrrolidone-5-carboxylate include N,N-diethyl-m-toluamide (DEET); N,N-diethylbenzamide; citronella; Tolu balsam; Peru balsam; Eucalyptus oil; Huon pine oil; camphor; cypress oil; galbanum; diethyl phthalate; dimethyl phthalate; dibutyl phthalate; 1,2,3a,4,5,5a,6,7,8,9,9a,9b-dodecahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b] furan; 4-(tricyclo [5.2.1.0<sup>2,6</sup>]decylidene-8) butanal; 1-ethoxy-1-(2'-phenylethoxy)ethane; acetyl cedrene and propylidene phthalide.

10

A composition according to the invention also comprises a mixture of menthyl 2-pyrrolidone-5-carboxylate and a second compound, said second compound having a repellency of at least 20% as determined by the insect repellency test defined in Example 1. Preferably, the second compound has a repellency of at least 40%, more preferably at least 50%, according to said test.

15

A further composition according to the invention comprises a mixture of menthyl 2-pyrrolidone-5-carboxylate and a second compound, said second compound being present in an amount which is sufficient to ensure that said second compound contributes to said composition an insect repellent effect equivalent to a repellency of at least 10% as determined by the insect repellency test defined in Example 1. Preferably, the second compound is present in said composition in an amount which is sufficient to ensure that said second compound contributes an insect repellent effect equivalent to a repellency of at least 20% as determined by said insect repellency test. More preferably, the insect repellent effect contributed by the second compound is equivalent to a repellency of at least 30%.

20

25

The invention is illustrated by the following non-limiting examples and by reference to Figure 1 which is a schematic representation of an apparatus suitable for testing compounds as insect repellents.

30



**EXAMPLE 1****Insect repellency test**

5 The effectiveness of menthyl 2-pyrrolidone-5-carboxylate as an insect repellent was tested using an apparatus similar to that disclosed in PCT Application WO 96/08147 and illustrated in Figure 1. The method is described for testing of menthyl 2-pyrrolidone-5-carboxylate but can be adapted to test any other compound in place of menthyl 2-pyrrolidone-5-carboxylate.

10 Four test chambers were prepared using 300 mm 200 gauge layflat tubing. The synthetic plastics tubing was attached to oblong stainless steel frames (150 mm by 150 mm by 900 mm) using double-sided adhesive tape. 200 mm squares of cotton netting were used to cover the ends of the chambers and were secured using adhesive tape.

15 Mosquitoes (naive insects of the species *Aedes aegypti*, 4 to 7 days old) were introduced into each chamber 8 and the chambers 8 were kept in a separate room until the test was ready to begin.

The exhaust fan which vents the room in which the test was performed was switched on.

20

Four targets 5 (only two shown) were prepared as follows: double layers of semi-porous membrane were stretched over the open ends of four open ended glassware bulbs (diameter of open end 43 mm) and secured using elastic bands. Testing was carried out at 27° C. The membranes were kept moist and warmed above the ambient temperature throughout the test by passing a supply of water (at 34° C) through the glassware bulbs, so as to contact the inner surface of the membranes.

25 Menthyl 2-pyrrolidone-5-carboxylate (30 microlitres) was applied to a membrane and spread as evenly as possible across the membrane surface. This was repeated with two other membranes and the fourth membrane was left untreated as a control.

30 The chambers 8 containing the mosquitoes were positioned so that each chamber had one netting end pressed against one of the targets 5. Glass partitions in the form of a cross 6 were used to separate each target 5 and chamber end from its neighbour.

35

600 mm 200 gauge layflat tubing was used to connect the various elements as shown in Figure 1, air was forced by an inlet fan (not shown) over the filters 2, 3, over the targets 5 and through the test chambers containing the mosquitoes. The separation of the

membranes ensured that air passing over a particular membrane would pass through only one test chamber 8.

5 The filters 2, 3 were used to remove volatile elements from the air passing over the mosquitoes; filter 2 contained activated charcoal and filter 3 contained a molecular sieve (Union Carbide type 5A zeolite). The material in each filter 2, 3 was held within the cells of a 25 mm thick sheet of aluminium honeycomb sandwiched between two sheets of stainless steel mesh held in an aluminium frame. The filters 2,3 were bolted by their frames to the inside of an aluminium tunnel such that air passing along the tunnel passed  
10 through the filters 2, 3.

Four cameras 9 (only two shown) positioned downwind of the test chambers 8 were each focused onto a particular target 5, and the images produced by the cameras displayed on a single monitor 15 by means of a quad splitter 13. An electronic timer was used to  
15 project the date and time onto the screen, and the video recorder 14 was used to record the data.

The mosquitoes in the test chambers 8 were activated by introduction of a human breath stimulus upwind of the targets 5 and the number of insects attempting to bite each  
20 target 5 over the next ten minute period was recorded. After ten minutes, the recording was stopped and the test chambers 8 removed from their position immediately downwind of the targets 5.

The targets 5 were left untouched (although still warmed and moistened) for one hour  
25 with the fans switched on, after which time the test chambers 8 were re-introduced and the test repeated to determine the repellency of the menthyl 2-pyrrolidone-5-carboxylate one hour after application.

The numbers of mosquitoes attempting to bite each of the targets 5 was noted every 10  
30 seconds throughout each ten minute recording period. The 60 readings were used to produce a figure for the mean number of insects biting each target 5 during the ten minute test periods. The reading obtained for the untreated target 5 was used to give a measure of the basic avidity of the mosquitoes used in the test and this was taken into account when analysing the results.

35

The standard insect repellent N,N-diethyl-m-toluamide (DEET) and menthol, one of the hydrolysis products of menthyl 2-pyrrolidone-5-carboxylate, were also tested using the

same apparatus for comparison with menthyl 2-pyrrolidone-5-carboxylate. The results are given in Table 1 below.

**TABLE 1**

5

Compound	% Repellency	
	Initially	After 1 Hour
Menthyl 2-pyrrolidone-5-carboxylate	80	59
DEET	93	75
Menthol	49	25

**EXAMPLE 2**

10 Compositions suitable for use in the invention include the following:

**A. Dry Oil Sprays**

	1	2
	% by weight	% by weight
PERFUME	20.00	14.60
CERAPHYL 375	18.00	14.60
ETHANOL	10.00	-
PERMETHYL 99A	50.00	68.80
MENTHYL 2-PYRROLIDONE-5-CARBOXYLATE (QUESTICE)	2.00	2.00

The menthyl 2-pyrrolidone-5-carboxylate was dissolved in the ethanol or permethyl and  
15 other ingredients were added with stirring.

## B. Body Lotion

		% by weight
PURIFIED WATER (a)		to 100.00
AMERCHOL L101	Mineral Oil & Lanolin Alcohol	8.50
DOW CORNING 1401	Cyclomethicone & Dimethiconol	4.00
QUESTICE L	Menthyl 2-pyrrolidone-5-carboxylate	1.50
ESTOL GMS (S/E) 1461	Glyceryl Stearate SE	1.50
STEARIC ACID		1.50
D-PANTHENOL 75L		1.00
TRIETHANOLAMINE		0.60
PEMULEN TR1	Acrylates/C10-30 Alkyl Acrylate	0.30
	Crosspolymer	
DOW CORNING 200/350	Dimethicone	0.20
NIPAGIN M	Methylparaben	0.20
NIPASOL M	Propylparaben	0.15
GERMALL 115	Imidazolidinyl Urea	0.15
PURIFIED WATER (b)		5.00
ALLANTOIN		0.10
PERFUME		q.s.

- 5 The Panthenol, Allantoin, Questice L were blended until the mixture was smooth and clear. The water and Nipagin were added and the mixture (water phase) was heated to 75° C. The Amerchol, Estol GMS, stearic acid, Dow Corning 200/350 and Nipasol were combined and heated to 75° C. The Pemulen was added to this mixture, ensuring that the temperature did not rise above 85° C, to form a slurry. The slurry was added to the
- 10 water phase and the resultant mixture was homogenised with addition of the triethanolamine until the product was smooth and lump-free. After cooling to 40° C with stirring, the Dow Corning 1401, Germall and water (b) were added and mixed in thoroughly.

## C. Moisturiser

		% by weight
PURIFIED WATER		to 100.00
FLORASUN 90	Sunflower Seed oil	10.00
BUTYLENE GLYCOL		4.00
SEPIGEL 305	Polyacrylamide & C13-14	1.60
	Isoparaffin & Laureth-7	
ARLACEL 165	Glyceryl Stearate & PEG-100 Stearate	2.50
ILLIPE BUTTER		2.00
DRY-FLO PLUS	Aluminium Starch Octenylsuccinate	2.00
QUESTICE L	Menthyl 2-pyrrolidone-5-carboxylate	1.70
FLORAESTERS-20	Jobaba Oil & Jobaba Wax	1.00
FLORAESTERS-30	Jobaba Oil & Jobaba Wax	1.00
PARSOL MCX	Octyl Methoxycinnamate	1.00
PONGAMIA EXTRACT	Pongamol	1.00
SPAN 60	Sorbitan Stearate	0.50
VITAMIN E ACETATE		0.50
D-PANTHENOL		0.50
PHENONIP	Phenoxyethanol & Methylparaben &	0.40
	Ethylparaben & Propylparaben &	
	Butylparaben	
NERVANAID BA2	Disodium EDTA	0.10
PERFUME		q.s.

- 5 The water and Nervanaid were combined and heated to 75° C (main batch). Separately the illipe butter, Floraesters, Florasun, Arlacel, Span, PONGAMIA EXTRACT and QUESTICE L were combined and heated to 75° C. The oils were added to the main batch with stirring, which was then cooled to 60° C and the Sepigel was added, homogenising until smooth and thick. After cooling to 45° C, the Butylene Glycol and
- 10 Dry-Flo were combined to make a slurry, and added to the main batch. After cooling to room temperature, the remaining ingredients were added.

## D. Foot Cream

		% by weight
PURIFIED WATER		to 100.00
CETYL ALCOHOL		3.00
SQUALENE		2.50
EMPILAN KM 20	Ceteareth 20	2.60
LIQUIWAX DIEFA	Diisoarachidyl Dilinoleate	2.50
SEPIGEL 305	Polyacrylamide & C13-14 Iso-paraffin & Laureth-7	2.00
QUESTICE	Menthyl 2-pyrrolidone-5-carboxylate	1.50
DOW CORNING 200/350	Dimethicone	0.80
NIPAGIN M	Methylparaben	0.20
NIPASOL M	Propylparaben	0.15
GERMALL 115	Imidazolidinyl Urea	0.15
PERFUME		q.s.

5 The water, Nipagin and Sepigel were combined and heated to 75° C. The oils were combined, heated to 75° C and added to the water phase with homogenising. The resultant mixture was cooled to room temperature with occasional stirring. The Germall was mixed with a little water, stirred until clear and added to the main batch.

## E. Liquid Talc

		% by weight
PURIFIED WATER		to 100.00
QUESTICE L	Menthyl 2-pyrrolidone-5-carboxylate	2.00
DOW CORNING 1401	Cyclomethicone & Dimethiconol	2.00
TALC		2.00
POLAWAX GP200	Cetearyl Alcohol & PEG-20 Stearate	1.50
ESTOL GTCC 3603	Capric/Caprylic Triglyceride	1.50
DRY-FLO PLUS	Aluminium Starch Octenylsuccinate	1.00
CETEARYL ALCOHOL	Lanette O	0.60
TRIETHANOLAMINE		0.50
CARBOPOL ULTREZ 10	Carbomer	0.20
SILKALL 100	Silk	0.20
EUXYL K400	Methyldibromo Glutaronitrile & Phenoxyethanol	0.20
PERFUME		q.s.

The Estol was added to the water, then the Carbopol was sprinkled on and allowed to wet out. The resultant mixture was heated to 65° C. The Cetearyl Alcohol, Polawax and Questice L were combined and heated to 65° C and added to the water phase with shear. While homogenisation continued the remaining ingredients were added, except the Euxyl, which was added cold.

#### F. Moisturising Gel

PHASE	INCI NAME	TRADE NAME	% by weight
A	Ceteareth-20	Empilan KM20	2.00
	Menthyl 2-pyrrolidone- 5-carboxylate	QUESTICE L	0.75
	QUEST PERFUME	AF 26689	0.20
	Ethanol		10.00
	Water (a)		10.00
	PEG-25 PABA	Uvinul P25	3.00
B	Carbomer (1% Soln.)	Carbopol 940	50.00
	Water (b)		to 100.00
	Imidazolidinyl Urea	Germall 115	0.20
	Patent Blue V	Blue V (0.5% Soln.)	0.10
	Panthenol	D-Panthenol 75l	0.75
	Sodium Hyaluronate		0.50
C	Triethanolamine		0.60

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The EMPILAN, QUESTICE L, QUEST PERFUME, UVINUL and ETHANOL were mixed together and once the mixture was homogenous, the WATER (a) was added. A solution of CARBOPOL was prepared and combined, in the main vessel, with WATER (b) and the remaining ingredients of phase B. To this gel, was added phase A in portions, mixing slowly but thoroughly between each addition.

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**EXAMPLE 3**

An insect repellent lotion was prepared to the following formulation.

		per cent by weight		
Phase A		A	B	C
Water		to 100.00	to 100.00	to 100.00
Glycerine		5.00	5.00	5.00
<b>Phase B</b>				
Dehyquart DAM	(i)	6.50	6.50	6.50
Petroleum Jelly	(ii)	7.00	7.00	7.00
DEET	(iii)	10.00	0.00	8.00
Crodamol IPP	(iv)	5.00	5.00	5.00
Cetyl Alcohol		3.00	3.00	3.00
Dow Corning 200/350	(v)	1.00	1.00	1.00
Questice™ L	(vi)	0.00	2.00	2.00
<b>Phase C</b>				
Phenonip	(vii)	0.60	0.60	0.60

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## INCI Names

- (i) Distearyl dimethyl ammonium chloride
- (ii) Petrolatum
- (iii) Diethyl toluamide
- (iv) Isopropyl palmitate
- (v) Dimethicone
- (vi) Menthyl PCA [2-pyrrolidone-5-carboxylate]
- (vii) Phenoxethanol

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- 15 Phases A and B were separately heated to 70° C and A was slowly added to B with shearing. The mixture was stirred until cool, then sheared again until completely homogenous. Finally Phase C was added with stirring.

- 20 The above lotions were tested for insect repellency using the method outlined in Example 1. The results are given below in Table 2.



15  
**TABLE 2**

	% Repellency	
	Initial	After 1 hour
Cream A	96	87
Cream B	64	44
Cream C	92	69

**CLAIMS**

1. The use of menthyl 2-pyrrolidone-5-carboxylate as an insect repellent.
2. The use of menthyl 2-pyrrolidone-5-carboxylate according to claim 1 in a composition which contains at least 0.05% menthyl 2-pyrrolidone-5-carboxylate by weight.
3. A method of repelling insects from an object or airspace comprising application to the object or into the airspace of an effective amount of menthyl 2-pyrrolidone-5-carboxylate.
4. The use of a perfumed composition comprising menthyl 2-pyrrolidone-5-carboxylate as an insect repellent.
5. The use of a perfumed composition according to claim 4 wherein said composition contains at least 0.05% by weight of menthyl 2-pyrrolidone-5-carboxylate.
6. The use of a composition according to any one of claims 2, 4 or 5 wherein said composition comprises a personal product, a cosmetic or a household product.
7. The use of a composition according to claim 6 wherein said composition comprises a fine fragrance, a cologne, a skin cream, a skin lotion, a deodorant, a talc, a bath oil, a soap, a shampoo, a hair conditioner, a styling agent, an air freshener, a hard surface cleaner or a laundry product.
8. The use of a composition according to claim 6 or 7 wherein said personal product, cosmetic or household product contains between 0.1 per cent and 10 per cent by weight of the composition used according to any one of claims 2, 4 or 5.
9. The use of a composition according to any one of claims 2 and 4 to 8 to repel biting insects, especially mosquitoes.
10. A composition for use as an insect repellent comprising a mixture of menthyl 2-pyrrolidone-5-carboxylate and a known insect repellent.

11. A composition according to claim 10 in which the known insect repellent is selected from the group consisting of N,N-diethyl-m-toluamide (DEET), N,N-diethylbenzamide, citronella, Tolu balsam, Peru balsam, Eucalyptus oil, Huon pine oil, camphor, cypress oil, galbanum, diethyl phthalate, dimethyl phthalate, dibutyl phthalate, 1,2,3a,4,5,5a,6,7,8,9,9a,9b-dodecahydro-3a,6,6,9a-tetramethyl-naphtho [2,1-b] furan, 4-(tricyclo [5.2.1.0<sup>2,6</sup>] decylidene-8) butanal, 1-ethoxy-1-(2'-phenylethoxy) ethane, acetyl cedrene and propylidene phthalide.
12. A composition for use as an insect repellent comprising a mixture of menthyl 2-pyrrolidone-5-carboxylate and a second compound, said second compound having a repellency of at least 20% as determined by the insect repellency test defined herein.
13. A composition according to claim 12 in which said second compound has a repellency of at least 40% as determined by the insect repellency test defined herein.
14. A composition according to claim 12 or 13 in which said second compound has a repellency of at least 50% as determined by the insect repellency test defined herein.
15. A composition for use as an insect repellent comprising a mixture of menthyl 2-pyrrolidone-5-carboxylate and a second compound, said second compound being present in an amount which is sufficient to ensure that said second compound contributes to said composition an insect repellent effect equivalent to a repellency of at least 10% as determined by the insect repellency test defined herein.
16. A composition according to claim 15 in which the amount of said second compound is sufficient to ensure that said second compound contributes to said composition an insect repellent effect equivalent to a repellency of at least 20% as determined by the insect repellency test defined herein.
17. A composition according to claim 15 or 16 in which the amount of said second compound is sufficient to ensure that said second compound contributes to said composition an insect repellent effect equivalent to a repellency of at least 30% as determined by the insect repellency test defined herein.

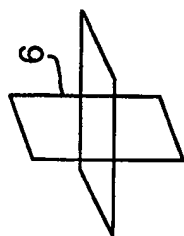
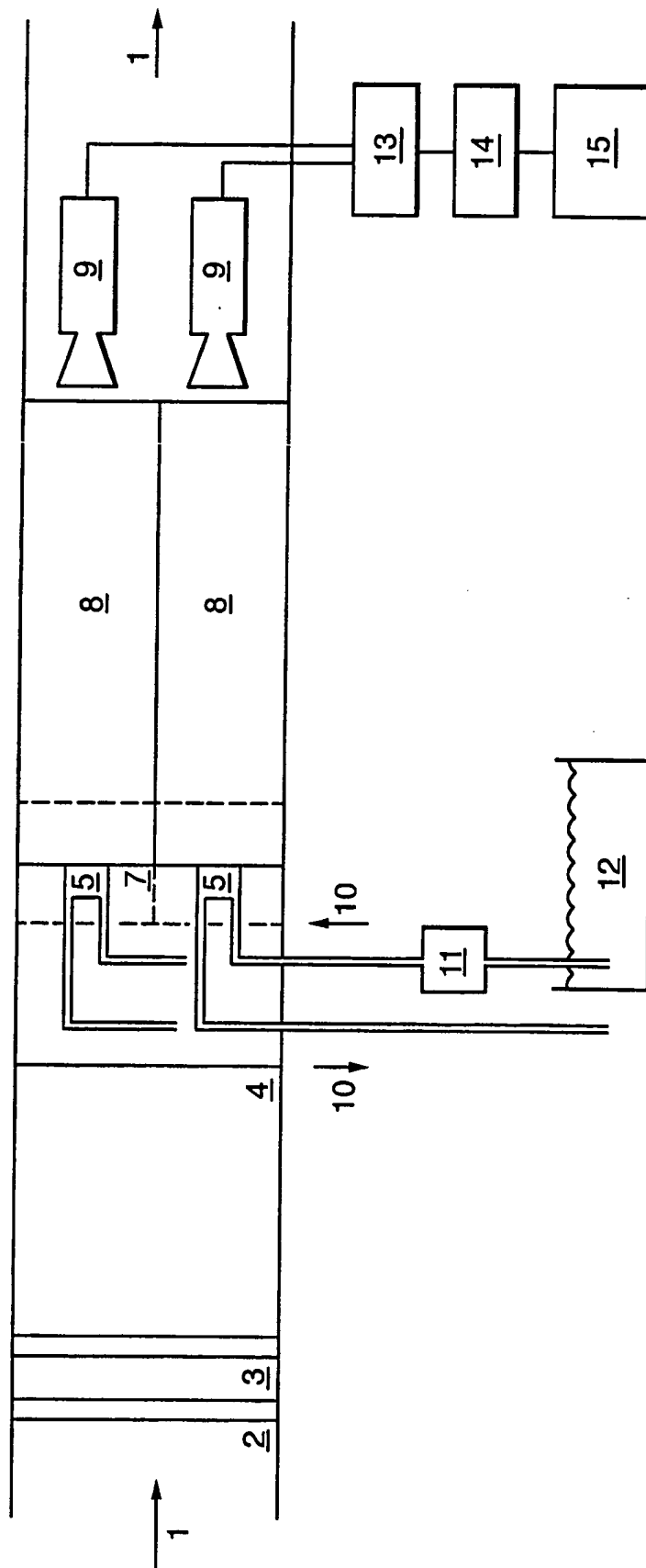


Fig.1.



## INTERNATIONAL SEARCH REPORT

Int. Application No.

PCT/GB 99/02808

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 A61K7/40 A01N43/36

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DATABASE WPI            Week 199515            Derwent Publications Ltd., London, GB;            AN 1995-110501            XP002123858            "Insecticide non-toxic to humans and animals - contains surfactant and water retaining space"            &amp; JP 07 033608 A (JAPAN TOBACCO),            3 February 1995 (1995-02-03)            abstract</p> <p style="text-align: center;">— —/—</p>	1, 12

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the International search

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## INTERNATIONAL SEARCH REPORT

Int. Patent Application No.

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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